PATENT
Customer Number 22,852
Attorney Docket No. 5552.1447

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Jürgen PATZKE	)	Group Art Unit: Unassigned
	)	
Serial No.: To be assigned	)	Examiner: Unassigned
	)	
Filed: Filed herewith	)	
	)	
For: INDUCED AGGREGATION AND AGGLUTINATION OF PLATELETS	)	

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to the examination of the above application, please amend this application as follows:

IN THE SPECIFICATION:

Please enter the following amended paragraph for the current paragraph at the bottom of page 4, top of page 5:

(Amended) Induction of macroaggregate formation is possible on use of various activators (Fig. 1). Such activators, such as, for example, ristocetin, collagen, ADP or epinephrine, are sufficiently well known to the person skilled in the area of platelet aggregation. A summary of the mode of functioning of various activators and their receptors is to be found, for example, in Blockmans D. et al. , Blood Review, 9, 1995, 143-156. The reaction kinetics of the formation of macroaggregates through

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Brownian diffusion vary widely for different activators. On the one hand, the frequency of collisions of microaggregates with other microaggregates or single platelets is crucial for macroaggregate formation. On the other hand, it is important that a collision is "successful", a part being played in turn by the state of activation, the charge condition, the size and number of the pseudopodia and many other parameters. Since the progress of activation brought about by the activators, also called agonists hereinafter, varies widely, it is understandable why in particular the result of macroaggregate formation varies widely, after stopping the stirrer, with the various agonists. The state or activation at the instant when the stirring is stopped is certainly an important parameter for the extent of the reaction proceeding thereafter.

IN THE CLAIMS:

Please cancel claims 1-17 without prejudice, and enter new claims 18-44 as follows:

18. A method of measuring the aggregation of blood platelets, comprising:

a) obtaining a sample;

b) adding reaction mixture ingredients to the sample thereby creating a reaction mixture;

c) mixing the reaction mixture in a first reaction phase; and

d) mixing the reaction mixture less vigorously or not at all in a second reaction phase and measuring the aggregation of blood platelets.

19. The method of claim 18, wherein the mixing is accomplished by stirring, shaking, vibrating, or ultrasound.

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20. The method of claim 19, wherein the stirring rate is between 200 and 2000 rpm.

21. The method of claim 18, wherein the blood platelets are physiologically active blood platelets.

22. The method of claim 18, wherein the the blood platelets are fixed blood platelets.

23. The method of claim 22, wherein platelet aggregation is measured using a ristocetin cofactor test.

24. The method of claim 18, wherein the sample is chosen from at least one of whole blood, platelet-rich plasma, diluted platelet-rich plasma, and purified platelets.

25. The method of claim 18, wherein measuring the aggregation of blood platelets is performed by one of turbidimetric, nephelometric or electromagnetic methods.

26. The method of claim 18, wherein a mixing time is determined by the particular reaction mixture ingredients used.

27. The method of claim 26, wherein the reaction mixture ingredients are platelet activators comprising ristocetin, collagen, ADP, epinephrine, or arachidonic acid.

28. A method of measuring the stability of blood platelet aggregates, comprising:

a) obtaining a sample;

b) adding reaction mixture ingredients to the sample thereby creating a first reaction mixture;

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c) mixing the first reaction mixture in a first reaction phase;

d) mixing the first reaction mixture less vigorously or not at all in a second reaction phase and measuring the aggregation of blood platelets in a first aggregation measurement;

e) repeating steps a) and b) to generate an analogous second reaction mixture;

f) mixing the second reaction mixture, wherein a second aggregation measurement is performed while mixing; and

g) comparing the first aggregation measurement to the second aggregation measurement.

29. The method of claim 28, wherein the mixing is accomplished by stirring, shaking, vibrating, or ultrasound.

30. The method of claim 29, wherein the stirring rate is between 200 and 2000 rpm.

31. The method of claim 28, wherein the blood platelets are physiologically active blood platelets.

32. The method of claim 28, wherein the the blood platelets are fixed blood platelets.

33. The method of claim 32, wherein platelet aggregation is measured using a ristocetin cofactor test.

34. The method of claim 28, wherein the sample is chosen from at least one of whole blood, platelet-rich plasma, diluted platelet-rich plasma, and purified platelets.

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35. The method of claim 28, wherein measuring the aggregation of blood platelets is performed by one of turbidimetric, nephelometric or electromagnetic methods.

36. The method of claim 28, wherein a mixing time is determined by the particular reaction mixture ingredients used.

37. The method of claim 36, wherein the reaction mixture ingredients are platelet activators comprising ristocetin, collagen, ADP, epinephrine, or arachidonic acid.

38. The method of claims 18 or 28, wherein the mixing of any reaction mixture is preceded by an incubation step without mixing.

39. The method of claim 38, wherein there is a sequence of multiple alternating mixing steps and non-mixing incubation steps.

40. The method of claims 18 or 28, wherein an initial aggregation measurement is taken before the reaction mixture is mixed.

41. The method of claims 18 or 28, wherein the aggregation measurements are determined by counting the remaining unaggregated platelets.

42. The method of claims 18 or 28, wherein the aggregation of blood platelets with other particles containing ligands or receptors that facilitate aggregation is measured.

43. The method of claims 18 or 28, wherein blood platelets may be replaced by any one of other cells, membrane vesicles, or artificial particles containing ligands or receptors that facilitate aggregation.

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44. The method of claims 18 or 28, wherein the mixing is adjusted to a lower intensity rather than completely stopped.

REMARKS

Applicant has amended the instant specification to correct the Blockmans reference page numbering from 143-1556 to 143-156. As this correction is inherent to the reference itself, Applicant contends that it does not represent new matter.

Applicant has canceled claims 1-17 and added new claims 18-44. Claims 18-44 are now pending in this case. Applicant has added claims 18-44 for the purpose of converting claims 1-17 to a format acceptable by the Office and to identify further inventions as supported by the instant specification. Applicant provides below a table indicating support in the specification for claims 18-44.

Claim(s)	Location of Specification Support
18	original claim 1; p. 4 lines 3-11
19	original claim 2; p.6 lines 6-9
20	p. 6 lines 14-17
21	original claim 3; p. 4 lines 5-7
22	original claim 4; p. 4 lines 5-7
23	original claim 4; p. 3 lines 25-31
24	original claim 5; p. 4 lines 12-13
25	original claims 6 and 7; p. 7 lines 1-6
26	original claim 8; p. 7 line 32 to p. 8 line 2
27	original claim 9; p. 4 lines 22-25; Figures 1a-1e
28	original claim 10; p. 7 lines 9-12
29	original claim 2; p.6 lines 6-9
30	p. 6 lines 14-17
31	original claim 3; p. 4 lines 5-7
32	original claim 4; p. 4 lines 5-7
33	original claim 4; p. 3 lines 25-31
34	original claim 5; p. 4 lines 12-13
35	original claims 6 and 7; p. 7 lines 1-6
36	original claim 8; p. 7 line 32 to p. 8 line 2
37	original claim 9; p. 4 lines 22-25; Figures 1a-1e
38	original claim 11; p. 7 lines 27-31
39	original claim 17; p. 7 lines 27-31

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Claim(s)	Location of Specification Support
40	original claim 12; Figures 1-4
41	original claim 13; p. 4 lines 12-13
42	original claim 14; p.8 lines 4-9
43	original claim 15; p. 1 lines11-16; p.8 lines 4-9
44	original claim 16; p. 5 lines 29-37

As support for claims 18-44 may be found in the instant specification, Applicant asserts that these claims do not constitute new matter.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: March 15, 2001

By: Carol P. Einaudi

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APPENDIX TO PRELIMINARY AMENDMENT OF MARCH 15, 2001

Amendments to the Specification

Induction of macroaggregate formation is possible on use of various activators (Fig. 1). Such activators, such as, for example, ristocetin, collagen, ADP or epinephrine, are sufficiently well known to the person skilled in the area of platelet aggregation. A summary of the mode of functioning of various activators and their receptors is to be found, for example, in Blockmans D. et al. , Blood Review, 9, 1995, 143-[1556] 156. The reaction kinetics of the formation of macroaggregates through Brownian diffusion vary widely for different activators. On the one hand, the frequency of collisions of microaggregates with other microaggregates or single platelets is crucial for macroaggregate formation. On the other hand, it is important that a collision is "successful", a part being played in turn by the state of activation, the charge condition, the size and number of the pseudopodia and many other parameters. Since the progress of activation brought about by the activators, also called agonists hereinafter, varies widely, it is understandable why in particular the result of macroaggregate formation varies widely, after stopping the stirrer, with the various agonists. The state or activation at the instant when the stirring is stopped is certainly an important parameter for the extent of the reaction proceeding thereafter.

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